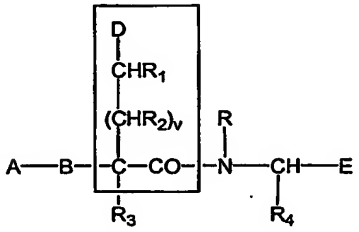
CLAIMS:

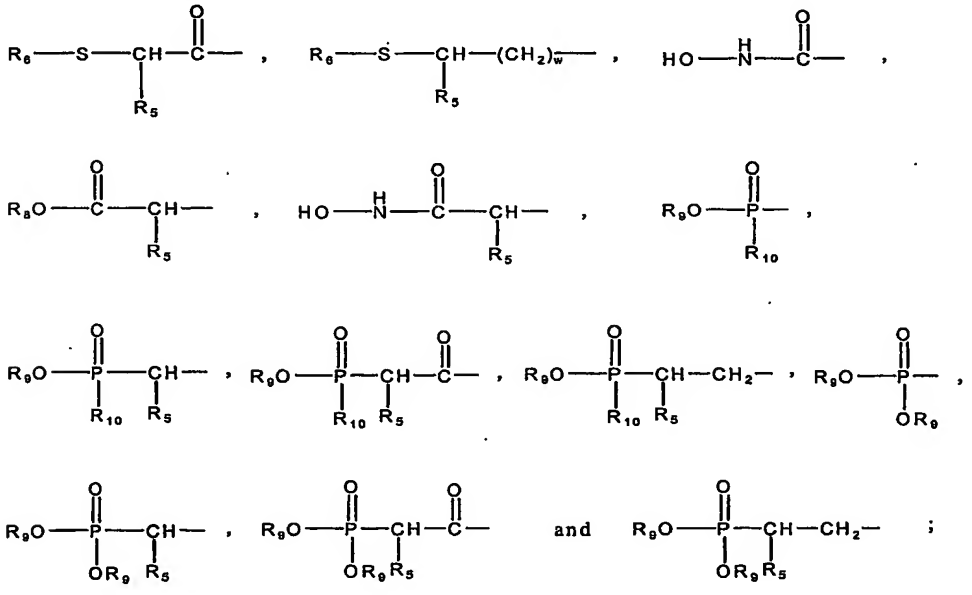
1. A compound of Formula (I), or a pharmaceutically acceptable salt thereof:

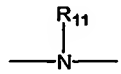


(I)

wherein:

A is a zinc ligand or zinc ligand bearing moiety selected from the group consisting of:



B is  , $-CH_2-$ or absent ;

R is hydrogen or lower alkyl ;

R_1 is hydrogen or lower alkyl ;

R_2 is hydrogen, or lower alkyl;

R_1, when v=1, may be connected to the carbon bearing R_2 to form an alkylene bridge of 1 carbon atom, representing with the carbon atom to which it is attached a cyclopropane ring;

R_2, when v=1, may be connected to the carbon bearing R_1 to form an alkylene bridge of 1 carbon atom representing with the carbon atom to which it is attached a cyclopropane ring;

R_3 is hydrogen or lower alkyl;

R_1, when v=1, may be connected to the carbon bearing R_3 to form an alkylene bridge of 1 carbon atom, representing with the carbon atom to which it is attached a cyclobutane ring;

R_3, when v=1, may be connected to the carbon bearing R_1 to form an alkylene bridge of 1 carbon atom, representing with the carbon atom to which it is attached a cyclobutane ring;

R_1 and R_3, when v=1, may be connected together to form an alkylene bridge of 2 carbon atoms representing with the carbon atoms to which they are attached a cyclopentane ring;

R_1 and R_3, when v=0, may be connected together to form an alkylene bridge of 3 carbon atoms representing with the carbon atoms to which they are attached a cyclopentane ring;

R_1 and R_3, when v=0, may be connected together to form an alkylene bridge of 4 carbon atoms representing with the carbon atoms to which they are attached a cyclohexane ring;

R_1 and R_3, when v=1, may be connected together to form an alkylene bridge of 3 carbon atoms representing with the carbon atoms to which they are attached a cyclohexane ring;

R_4 is lower alkyl, substituted lower alkyl, cycloalkyl-$(CH_2)_w$-, aryl-$(CH_2)_w$-, substituted aryl –$(CH_2)_w$- or heteroaryl-$(CH_2)_w$-;

R and R_4 may be connected together to form an alkylene bridge of 3 carbon atoms representing with the nitrogen and carbon atoms to which they are attached a pyrrolidine ring;

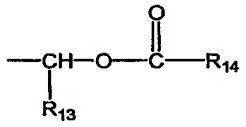
R and R_4 may be connected together to form an alkylene bridge of 4 carbon atoms representing with the nitrogen and carbon atoms to which they are attached a piperidine ring;

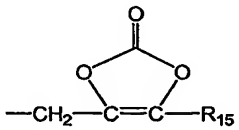
R_5 is hydrogen, lower alkyl, substituted lower alkyl, cycloalkyl-$(CH_2)_x$-, aryl-$(CH_2)_x$-, substituted aryl-$(CH_2)_x$-, or heteroaryl-$(CH_2)_x$-;

R_6 is hydrogen, R_7-CO-, or R_{12}-S-;

R_7 is alkyl, substituted alkyl, cycloalkyl-$(CH_2)_y$, aryl-$(CH_2)_y$-, substituted aryl-$(CH_2)_y$- or heteroaryl-$(CH_2)_y$-;

R_8 and R_9 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, aryl-$(CH_2)_y$-, substituted aryl-$(CH_2)_y$-, heteroaryl-$(CH_2)_y$-,



and


;

R_{10} is alkyl, substituted alkyl, cycloalkyl-$(CH_2)_y$, aryl-$(CH_2)_y$-, substituted aryl-$(CH_2)_y$- or heteroaryl-$(CH_2)_y$-;

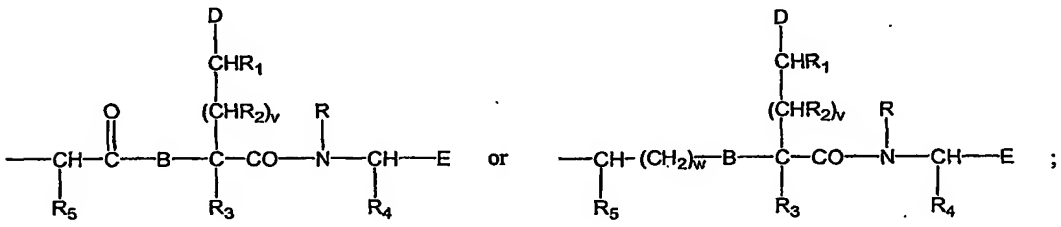
R_{11} is hydrogen or lower alkyl; wherein the carbon bearing R_1 and the nitrogen bearing R_{11}, when v=1, may be directly connected together to form an azetidine ring;

R_1 and R_{11}, when v=0, may be connected together to form an alkylene bridge of 3 carbon atoms representing with the nitrogen and carbon atoms to which they are attached a piperidine ring;

R_1 and R_{11}, when v=1, may be connected together to form an alkylene bridge of 2 carbon atoms representing with the nitrogen and carbon atoms to which they are attached a piperidine ring;

R_2 and R_{11}, when v=1, may be connected together to form an alkylene bridge of 2 carbon atoms representing with the nitrogen and carbon atoms to which they are attached a pyrrolidine ring; the alkylene bridge may be substituted by a lower alkyl or alkenyl group at either carbon;

R_{12} is alkyl, substituted alkyl, cycloalkyl-$(CH_2)_y$-, aryl-$(CH_2)_y$-, substituted aryl-$(CH_2)_y$-, heteroaryl-$(CH_2)_y$-,



in which case –S-R_{12} completes a symmetrical disulfide;

R_{13} is hydrogen, lower alkyl, cycloalkyl or phenyl;

R_{14} is hydrogen, lower alkyl, lower alkoxy or phenyl;

R_{15} is lower alkyl or aryl-$(CH_2)_y$-;

D is –COOH, -SO_2H, -SO_3H, –PO_3H_2; -OSO_3H or –OPO_3H_2;

E is hydrogen, R_{12}, -COOH, -$CONH_2$, -CONH(lower alkyl), -CON(lower alkyl)$_2$, -CONH-$(CH_2)_z$-aryl, -CON(-$(CH_2)_z$-aryl)$_2$, -CO-amino acid, -CH_2COOH, CH_2OH, -CH_2CH_2OH, or –$COOR_{16}$;

R_{16} is as previously defined for R_8 and R_9;

C is carbon;

H is hydrogen;

O is oxygen;

N is nitrogen;

S is sulfur;
P is phosphorus;
v is zero or one;
w is zero or an integer ranging from 1 to 4;
x is an integer ranging from 1 to 4;
y is zero or an integer ranging from 1 to 6; and
z is zero, one, two or three.

2. The compound as defined in claim 1, which is:
N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-(2-mercapto-acetylamino)- succinamic acid;
N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-(2-mercapto-3-phenyl-propionyl amino)-succinamic acid;
N-[1-Carboxy-2-(1*H*-indol-3-yl)-ethyl]-3-(2-mercapto-propionylamino)-succinamic acid;
N-[1-Carboxy-2-(1*H*-indol-3-yl)-ethyl]-3-(2-mercapto-4-methyl-pentanoylamino)-succinamic acid;
N-[1-Carboxy-2-(1*H*-indol-3-yl)-ethyl]-3-(2-mercapto-3-methyl-butyrylamino)-succinamic acid;
N-[1-Carboxy-2-(1*H*-indol-3-yl)-ethyl]-3-(3-hydroxy-2-mercapto-propionylamino)-succinamic acid;
N-[1-Carboxy-2-(1*H*-indol-3-yl)-ethyl]-3-(3-hydroxy-2-mercapto-butyrylamino)-succinamic acid;
N-[1-Carboxy-2-(1*H*-indol-3-yl)-ethyl]-3-(2-mercapto-hexanoylamino)-succinamic acid;
N-[1-Carboxy-2-(1*H*-indol-3-yl)-ethyl]-3-(2-mercapto-4-phenyl-butyrylamino)-succinamic acid;
N-[1-Carboxy-2-(1*H*-indol-3-yl)-ethyl]-3-(2-mercapto-2-phenyl-acetylamino)-succinamic acid;
3-(3-Biphenyl-4-yl-2-mercapto-propionylamino)-*N*-[1-Carboxy-2-(1*H*-indol-3-yl)-ethyl]-succinamic acid;

3-(3-(4-Benzyloxy-phenyl)-2-mercapto-propionylamino)-*N*-[1-Carboxy-2-(1*H*-indol-3-yl)-ethyl]-succinamic acid;

N-[1-Carboxy-2-(1*H*-indol-3-yl)-ethyl]-3-[3-(4-fluoro-phenyl)-2-mercapto-propionylamino]-succinamic acid;

N-[1-Carboxy-2-(1*H*-indol-3-yl)-ethyl]-3-[2-mercapto-3-(4-methoxy-phenyl)-propionylamino]-succinamic acid;

N-[1-Carboxy-2-(1*H*-indol-3-yl)-ethyl]-3-(3-cyclohexyl-2-mercapto-propionylamino)-succinamic acid;

N-[1-Carboxy-2-(1*H*-indol-3-yl)-ethyl]-3-[3-(1*H*-indol-3-yl)-2-mercapto-propionylamino]-succinamic acid;

N-[1-Carboxy-2-(1*H*-indol-3-yl)-ethyl]-3-(2-mercapto-3-naphthalen-2-yl-propionylamino]-succinamic acid;

N-(1-Carboxy-2-naphthalen-2-yl-ethyl)-3-(2-mercapto-3-phenyl propionylamino)-succinamic acid;

N-(1-Carboxy-2-hydroxy-ethyl)-3-(2-mercapto-3-phenyl-propionyl amino)-succinamic acid;

N-[1-Carboxy-2-(4-hydroxy-phenyl)-ethyl]-3-(2-mercapto-3-phenyl-propionylamino)-succinamic acid;

N-[1-Carboxy-2-phenyl-ethyl)-3-(2-mercapto-3-phenyl-propionyl amino)-succinamic acid;

N-(2-Biphenyl-4-yl-1-Carboxy-ethyl)-3-(2-mercapto-3-phenyl-propionyl amino)-succinamic acid;

N-(1-Benzyl-2-hydroxy-ethyl)-3-(2-mercapto-3-phenyl-propionyl amino)-succinamic acid;

N-[1-Carboxy-2-(1*H*-indol-3-yl)-ethyl]-3-(2-mercapto-3-phenyl-propionylamino)-succinamic acid;

4-[1-Carboxy-2-(1*H*-indol-3-yl)-ethylcarbamoyl]-4-(2-mercapto-3-phenyl-propionylamino)-ethyl]-butyric acid;

N-[2-(1*H*-indol-3-yl)-methylcarbamoyl-ethyl]-3-(2-mercapto-acetyl amino)-succinamic acid;

N-[1-(1-Carboxy-2-hydroxy-ethylcarbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-3-(2-mercapto-3-phenyl-propionylamino)-succinamic acid;

N-[2-(1*H*-indol-3-yl)-methoxycarbonyl-ethyl]-3-(2-mercapto-acetyl amino)-succinamic acid;

N-[2-(1*H*-indol-3-yl)l-ethyl]-3-(2-mercapto-3-phenyl-propionylamino)-succinamic acid;

3-(2-Biphenyl-4-yl-ethylcarbamoyl)-4-hydroxycarbamoyl-butyric acid;

3-[2-(4'-Cyano-biphenyl-4-yl)-ethylcarbamoyl]-4-hydroxycarbamoyl-butyric acid;

4-Hydroxycarbamoyl-3-[2-(4-pyridin-2-yl-phenyl)-ethylcarbamoyl]-butyric acid;

4-Hydroxycarbamoyl-3-(4-phenyl-butylcarbamoyl)-butyric acid;

4-Hydroxycarbamoyl-3-(2-phenoxy-ethylcarbamoyl)-butyric acid;

3-[2-(4'-Hydroxy-biphenyl-4-yl)-ethylcarbamoyl]-4-hydroxycarbamoyl-butyric acid;

3-(2,2-Diphenyl-ethylcarbamoyl)-4-hydroxycarbamoyl-butyric acid;

3-[2-(4'-Dimethylamino-biphenyl-4-yl)-ethylcarbamoyl]-4-hydroxycarbamoyl-butyric acid;

4-Hydroxycarbamoyl-3-(5-hydroxy-pentylcarbamoyl)-butyric acid;

3-[(Biphenyl-4-ylmethyl)-carbamoyl]-4-hydroxycarbamoyl-butyric acid;

3-(2-Biphenyl-4-yl-ethylcarbamoyl)-5-hydroxycarbamoyl-pentanoic acid;

N-[1-carboxy-2-(1H-indol-3-yl)-ethyl]-3-(3-phenyl-1-phosphono-propylamino)-succinic acid; or

3-(2-Naphthalen-2-yl-ethylcarbamoyl)-pentanedioic acid.

3. The compound of claim 2, which is 3-(2-Biphenyl-4-yl-ethylcarbamoyl)-4-hydroxycarbamoyl-butyric acid.

4. A pharmaceutical composition comprising a therapeutically effective amount of a compound of any one of claims 1 to 3 and a physiologically acceptable carrier or excipient.

5. A method for inhibiting PHEX comprising contacting PHEX with an inhibitory amount of a compound as recited in any one of claims 1 to 3.

6. A method for stimulating bone mass formation in a mammal comprising inhibiting PHEX with an effective amount of a compound as recited in any one of claims 1 to 3.

7. A method for treating or preventing a disease or condition associated with a phosphate metabolism defect comprising administering an effective amount of a compound as recited in any one of claims 1 to 3 to a mammal in need thereof.

8. A method as recited in claim 7, wherein said disease or condition is selected from the group consisting of hyperphosphatemia, hyperparathyroidism and renal insufficiencies.

9. A method for identifying PHEX substrates comprising

contacting a candidate with PHEX in the presence and in the absence of a compound as recited in any one of claims 1 to 3; and

assessing PHEX biological activity on the candidate in the presence and in the absence of the compound,

wherein the candidate compound is selected as a PHEX substrate when PHEX biological activity is measurably higher in the absence versus in the presence of the compound.

10. A use of a compound as recited in any one of claims 1 to 3 for inhibiting PHEX.

11. A use of a compound as recited in any one of claims 1 to 3 for stimulating bone mass formation in a mammal.

12. A use of a compound as recited in any one of claims 1 to 3 for treating or preventing a disease or condition associated with a phosphate metabolism.

13. A use of a compound as recited in claim 12, wherein said disease or condition is selected from the group consisting of hyperphosphatemia, hyperparathyroidism and renal insufficiencies.

14. A use of a compound as recited in any one of claims 1 to 3, for identifying PHEX substrates comprising

contacting a candidate with PHEX in the presence and in the absence of the compound; and

assessing PHEX biological activity on the candidate in the presence and in the absence of the compound,

wherein the candidate compound is selected as a PHEX substrate when PHEX biological activity is measurably higher in the absence versus in the presence of the compound.